Environmental Stewardship of PPCPs

◂ The *Green Pharmacy* ▸

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U.S. EPA Notice

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Citing this Presentation

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Also note that this archived version of the original presentation shows a number of imbedded GIF files. In the original PowerPoint presentation from which this Acrobat file was created, these GIFs were animated. In this PDF version, however, only a random still frame is displayed for each animated GIF and may not make sense in the absence of the animation.

Wealth of materials and links for:
Environmental Stewardship of PPCPs
at the U.S. EPA's web page on the
Green Pharmacy:

http://www.epa.gov/nerlesd1/chemistry/ppcp/greenpharmacy.htm

Note: This slide show is intended as a supplement to the documents and materials available at the *Green Pharmacy* web page. While some of the materials presented here are new, most of the concepts are more fully developed in those documents.

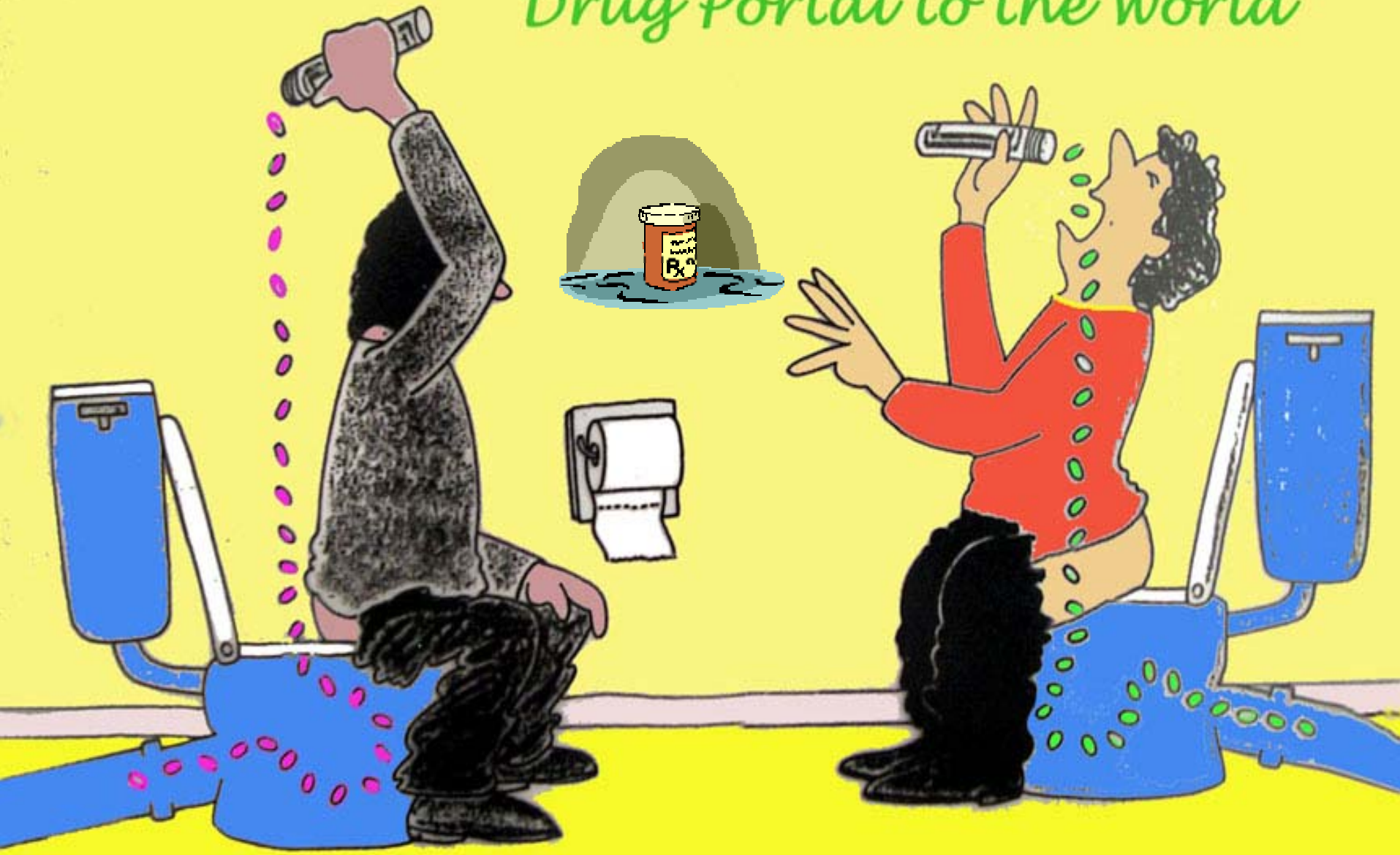
What's the Issue?

Pharmaceuticals and personal care products (**PPCPs**) are trace environmental pollutants resulting directly from …

the collective, but individually minuscule, actions and activities of individuals (and domestic animals) worldwide.

Their primary routes to the environment are excretion, washing, and direct disposal.

Drug Portal to the World

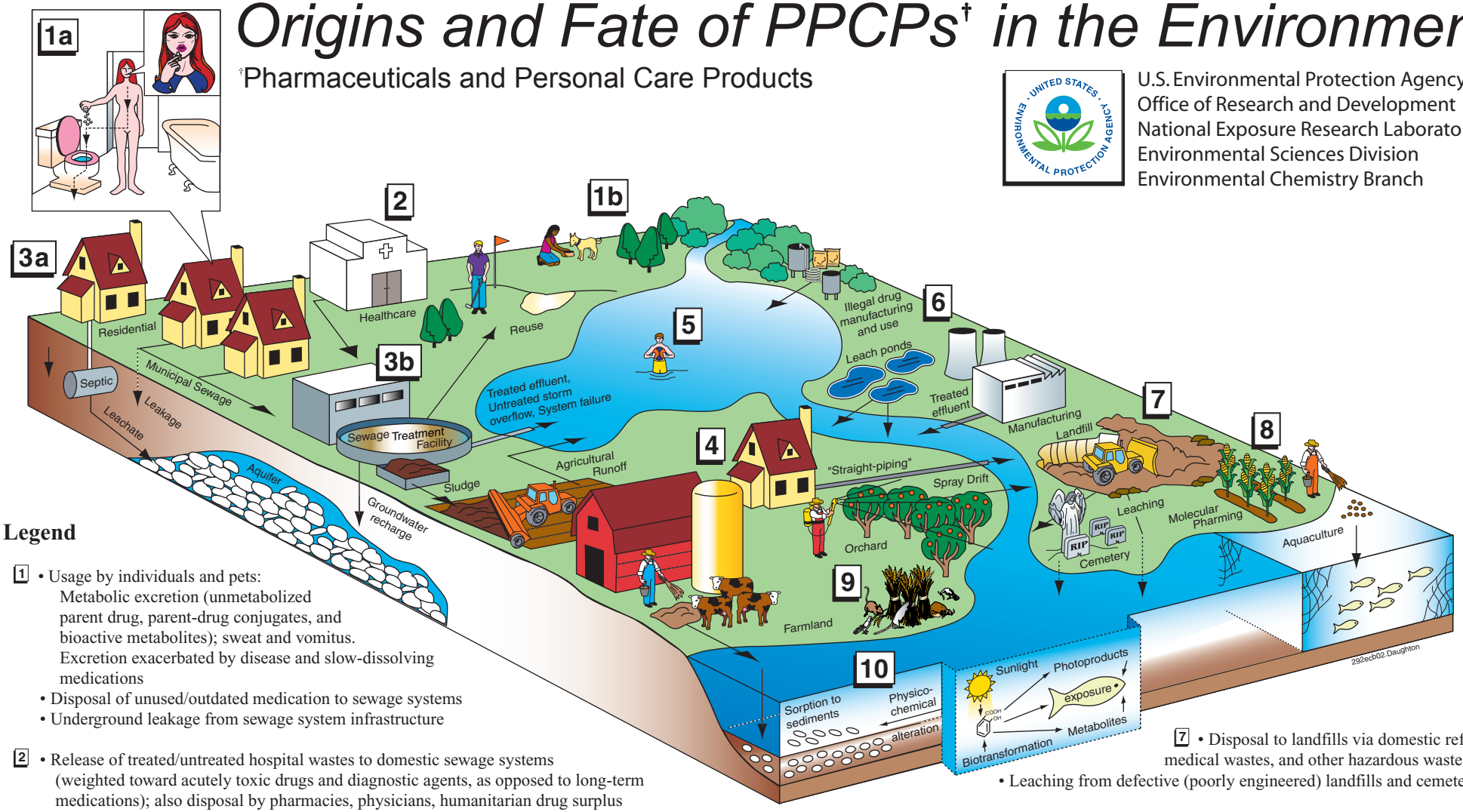


adapted by Daughton from Ternes (April 2000)

Origins and Fate of PPCPs† in the Environment

†Pharmaceuticals and Personal Care Products

U.S. Environmental Protection Agency
Office of Research and Development
National Exposure Research Laboratory
Environmental Sciences Division
Environmental Chemistry Branch



Legend

1 • Usage by individuals and pets:
Metabolic excretion (unmetabolized parent drug, parent-drug conjugates, and bioactive metabolites); sweat and vomitus.
Excretion exacerbated by disease and slow-dissolving medications
• Disposal of unused/outdated medication to sewage systems
• Underground leakage from sewage system infrastructure

2 • Release of treated/untreated hospital wastes to domestic sewage systems (weighted toward acutely toxic drugs and diagnostic agents, as opposed to long-term medications); also disposal by pharmacies, physicians, humanitarian drug surplus

3 • Release to private septic/leach fields
• Treated effluent from domestic sewage treatment plants discharged to surface waters or re-injected into aquifers (recharge)
• Overflow of untreated sewage from storm events and system failures directly to surface waters

4 • Transfer of sewage solids ("biosolids") to land (e.g., soil amendment/fertilization)
• "Straight-piping" from homes (untreated sewage discharged directly to surface waters)
• Release from agriculture: spray drift from tree crops (e.g., antibiotics)
• Dung from medicated domestic animals (e.g., feed) - CAFOs (confined animal feeding operations)

5 • Direct release to open waters via washing/bathing/swimming

6 • Discharge of regulated/controlled industrial manufacturing waste streams
• Disposal/release from clandestine drug labs and illicit drug usage

7 • Disposal to landfills via domestic refuse, medical wastes, and other hazardous wastes
• Leaching from defective (poorly engineered) landfills and cemeteries

8 • Release to open waters from aquaculture (medicated feed and resulting excreta)
• Future potential for release from molecular pharming (production of therapeutics in crops)

9 • Release of drugs that serve double duty as pest control agents:
examples: 4-aminopyridine, experimental multiple sclerosis drug → used as avicide; warfarin, anticoagulant → rat poison; azacholesterol, antilipidemics → avian/rodent reproductive inhibitors; certain antibiotics → used for orchard pathogens; acetaminophen, analgesic → brown tree snake control; caffeine, stimulant → *coqui* frog control

10 Ultimate environmental fate:
• most PPCPs eventually transported from terrestrial domain to aqueous domain
• phototransformation (both direct and indirect reactions via UV light)
• physicochemical alteration, degradation, and ultimate mineralization
• volatilization (mainly certain anesthetics, fragrances)

Christian G. Daughton, U.S. EPA-Las Vegas

February 2001 (revised July 2002)

http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm

Objectives of this Work

- Present an overview and background for the topic: *Environmental Stewardship of Pharmaceuticals and Personal Care Products — The Green Pharmacy.*
- Catalyze and promote an inter-disciplinary discussion and exploration of new ideas for moving toward a *Green Pharmacy.*
- Emphasize true, holistic "cradle-to-cradle" approaches for minimizing environmental impact of PPCPs while at the same time improving medical healthcare outcomes for consumers and reducing healthcare costs.

Importance of Forging Collaborations between Environmental Scientists & Medical Community

- Existing literature almost exclusively a result of efforts from environmental scientists (primarily analytical chemists).
- Much could be contributed from the many fields of medical science and healthcare practice.
- Cross-communication and collaborations would prove extremely useful.

- Partly in an attempt to catalyze inter-disciplinary efforts, the British medical journal *The Lancet* published a commentary that introduced this topic to the medical community:

"Environmental stewardship and drugs as pollutants"
(C.G. Daughton), *The Lancet*, **2002**, *360*:1035-1036

Potential Outcomes

- Foster development of consistent nationwide guidance/regulations for disposal or re-use of PPCPs.
- Change in consumer behavior and values regarding PPCP consumption (via outreach programs and education, including a re-designed use of direct-to-consumer [DTC] advertising). Raise public awareness of the environmental ramifications of their consumption decisions.
- Accelerate continued advancements by manufacturers and health care industry in more environmentally sound chemical design, manufacturing, packaging, marketing, distribution, purveyance, and therapeutic delivery.
- Ultimately, these outcomes could potentially lead to:

  Improved health care end points
  Lessen total medication expense and other health care costs
  Reduce the potential for environment impact

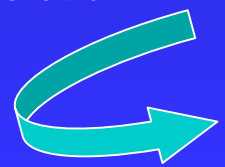
Actions in the Absence of Knowledge

- Even in the absence of knowledge regarding the impact of numerous PPCPs at trace concentrations in the environment, a wide spectrum of preventative actions and measures could be taken to minimize the introduction of PPCPs to the environment.
- "Cradle-to-cradle" design and stewardship would be appropriate under the *Precautionary Principle*.
- Existing and innovative approaches for stewardship can span the spectrum from time of PPCP discovery, design, manufacturing, packaging, and distribution, to purveyance, use, and disposal/recycling.
- Pollution prevention and waste minimization would be targeted for both the health care industry and consumer sector.

"Cradle-to-Cradle" Design and Stewardship

"Cradle-to-cradle" design & stewardship combines the factors already embodied in a wide range of other concepts and programs such as:

- **zero waste**
- **zero emissions**
- **waste-to-wealth**
- **green chemistry**
- **eco-effectiveness**
- **industrial ecology**
- **waste minimization**
- **product-stewardship**
- **ecological intelligence**
- **pollution prevention (P2)**
- **design for the environment (DfE)**
- **life cycle planning/design/assessment (LCA)**
- **extended product responsibility (EPR)** (including not just the producer, but rather the entire use-chain, including consumer)
- **product "take-back" programs** (where unused/unneeded product travels back up through the distribution chain — "reverse distribution")
- ... and many others.



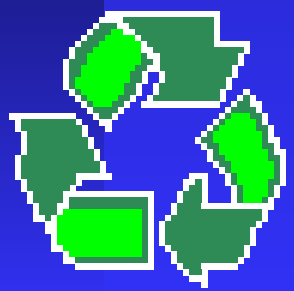
"Cradle-to-Cradle" Design and Stewardship

A cradle-to-cradle approach emphasizes managing the life-cycle flow of materials ...

always with the objective of seizing new opportunities to lessen environmental impact ...

while at the same time improving conditions for individuals, society, and industry.

Managing all materials as perpetual resources rather than eventually as wastes.



"Cradle-to-Cradle" Design and Stewardship

The many, complex aspects of this topic are covered in a holistic manner for the first time in a two-part paper in *Environmental Health Perspectives*:

"Cradle-to-Cradle Stewardship of Drugs for Minimizing Their Environmental Disposition while Promoting Human Health —"

Part I: *Rationale and Avenues toward a Green Pharmacy*

&

Part II: *Drug Disposal, Waste Reduction, and Future Direction*

Daughton CG. Accepted Oct. 2002. On-Line Dec. 2002.

Available:

http://www.epa.gov/nerlesd1/chemistry/ppcp/greenpharmacy.htm

Collateral Benefits
– *Cradle-to-Cradle Stewardship* –

- A wide array of activities and efforts centered on pollution prevention (source reduction, minimization, elimination) could have significant consequences for improved consumer health and economy. These pollution prevention efforts fall under the umbrella of "Cradle-to-Cradle Stewardship." Most of these actions would originate from a broad range of sectors in the healthcare industry but some would also originate with the consumer.

- Design and implementation of a successful voluntary compliance approach to life-cycle stewardship of PPCPs (a holistic "cradle-to-cradle" approach) could not only minimize any potential for adverse environmental impact, but **could also improve medical healthcare outcomes and consumer safety as well as reduce healthcare costs.**

"Disclaimer" and Caveats: The Linkage Between the Consumer and the Healthcare Community with the Environment

A wide and perhaps seemingly unrelated collection of issues involving a broad spectrum of actions and behaviors associated with the usage of PPCPs by consumers and the larger healthcare community are presented in this slide show. These issues are presented as examples of the enormous range and complexity of the countless dimensions involved with the life-cycles of PPCPs.

Each of these examples was selected merely as representative of myriads of others. No examination has ever been made as to which (if any) of these actions or others might prove to be effective at controlling environmental pollution. Nor are implications of priorities made. After all, there are a wide range of factors that determine whether any particular PPCP even has the potential to enter the environment (see: http://www.epa.gov/nerlesd1/chemistry/pharma/slides/part3.pdf); if a particular PPCP has little potential for being introduced to the environment, little can be gained by attempts at preventing pollution.

The connections between the examples presented here and how these examples might affect the ultimate disposition of PPCPs in the environment may not be immediately apparent without closer examination. But in the final analysis, each of these actions is tied to at least some of the multitude of factors that dictates how PPCPs enter the environment in general. By modifying these processes, it could prove possible to control pollution from PPCPs while also effecting improvements in health care — this is one of the distinguishing factors of "cradle-to-cradle" stewardship.

Grand Challenges in Environmental Sciences

The National Research Council (as requested by the National Science Foundation) synthesized the broad expertise from across the many disciplines embodied in environmental science to offer its judgment as to the ***most significant environmental research challenges of the next generation*** – based on their "potential to provide a scientific breakthrough of practical importance to humankind if given major new funding".

Of the eight "grand challenges" identified in the NRC's report (*Grand Challenges in Environmental Sciences*[†]), two require concerted input from those involved with pollutant identification: (1) "Hydrologic Forecasting" (for predicting changes in freshwater resources as a result in part of chemical contamination) and (2) "**Reinventing the Use of Materials**".

[†] National Research Council. *Grand Challenges in Environmental Sciences*; Committee on Grand Challenges in Environmental Sciences, Oversight Commission for the Committee on Grand Challenges in Environmental Sciences, National Academy Press: Washington, DC, 2000, 88 pp. (Prepublication stage) [available: http://www.nap.edu/books/0309072549/html/]

Grand Challenges in Environmental Sciences
(continued)

The impetus driving the second ("Reinventing the Use of Materials") is:

"…new compounds and other substances are constantly being incorporated into modern technology and hence into the environment, with insufficient thought being given to the implications of these actions. All of these issues assume added importance in urban areas, which concentrate flows of resources, generation of residues, and environmental impacts within spatially constrained areas. From a policy standpoint, reliable predictive models of material cycles could be invaluable in guiding decisions about ... topics relating to human-environment interactions..."

"**This grand challenge centrally encompasses questions about societal-level consumption patterns, since consumption is the primary force driving human perturbations of material cycles**."

Types of actions that could be implemented and others already underway for making progress toward a *Green Pharmacy* …


KINGsize! Medication
Over 81 kg (179 lbs) of
acetaminophen, ibuprofen, and aspirin
(just in these 20 cases)
NIGHT-TIME
PAIN RELIEVER
IBUPROFEN

NSAIDs Illustrate Problems with Inadvertent Overusage

[note that although acetaminophen is not an NSAID (as it is not an anti-inflammatory), it is often loosely lumped under the NSAID category]

Few consumers appreciate that:

- Every NSAID (like any drug) has a maximum safe: unit dose, cumulative daily dose, and duration of dosage (in the absence of physician oversight, generally 1-2 weeks).
- Recommended time courses can be overlooked; leads to unsafe continuous exposures.
- Different products from different manufacturers (for the same/different intended therapies) containing same active ingredient can lead to unsafe cumulative exposure.
- Safe, recommended doses of any particular NSAID can be easily exceeded even when following prudent/safe-use instructions. This results from aggregate exposure (ingesting another medication containing the same active ingredient), for which label warnings do not exist.
- Many individual formulations contain the maximum safe dosage. Unwitting cumulative exposure via consumption of multiple formulations can lead to overdosage.
- Different formulations from same manufacturer can contain different amounts of active ingredient, leading to confusion regarding total amount ingested. For example, different products from a single manufacturer can contain acetaminophen in dosage amounts of: 80, 160, 325, 500, 650, or 1,000 milligrams.

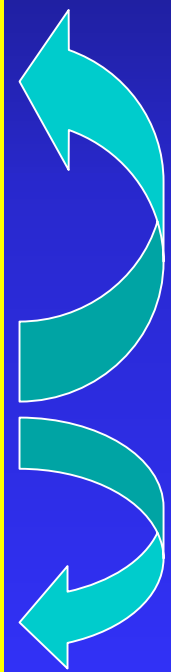
Acetaminophen formulations from a single OTC brand name

OTC Brand Name Acetaminophen: Individual Formulations from a Single Manufacturer

formulation name	dose (mg) per unit measure	unit measure
Adult Formulation		
Pain: Regular Strength	325	pill
Cold	325	pill
Pain: Extra Strength	500	pill
Pain and sleeplessness	500	pill
Flu	500	pill
Women's Menstrual Relief	500	pill
Sinus	500	pill
Allergy	500	pill
Arthritis Pain: Extended Relief	650	pill
Maximum Strength Sore Throat	1,000	2 tablespoons
Flu	1,000	2 tablespoons
Child/Infant Formulation		
Children's Chewable	80	pill
Children's Cold Chewable	80	pill
Children's Cold + Cough Chewable	80	pill
Junior Strength Chewable	160	pill
Infants' Concentrated Drops	160	2 droppers full (1.6 mL)
Infants' Cold Concentrated Drops	160	2 droppers full (1.6 mL)
Infants' Cold + Cough Concentrated Drops	160	2 droppers full (1.6 mL)
Children's Suspension Liquid	160	teaspoon (5 mL)
Children's Flu	160	teaspoon (5 mL)
Children's Sinus	160	teaspoon (5 mL)
Children's Cold Liquid	160	teaspoon (5 mL)
Children's Cold + Cough Liquid	160	teaspoon (5 mL)
Children's Allergy	160	teaspoon (5 mL)

Consumer confusion can lead to excessive doses

- 11 distinct adult formulations
- 13 distinct child formulations



- if an adult used 2 tablespoons of “Infants' Concentrated Drops,” this would give a toxic dose of 2,960 mg
- if “Infants' Concentrated Drops” were used for a child, 1 teaspoon would give a toxic 500-mg dose

Aggregate Dosing of NSAIDs

- Survey (2003, *National Consumers League*) reports that as a result of NSAID use, 16,500 Americans die each year and 103,000 are hospitalized from NSAID-related complications.
- Of America adults, 84% used NSAIDs in 2002, and 44% knowingly exceeded recommended doses.
- Of those taking OTC NSAIDs:

  45% agreed that it is safe to take an OTC pain reliever while also taking another OTC cold/flu medication (which probably contains an NSAID).

  34% agreed it is safe to take an OTC pain reliever while taking a prescription medication (which might contain an NSAID)
- Unknown as to what percentage of adults willingly and/or inadvertently consume excessive aggregate doses of NSAIDs from multiple sources.

From: "New Survey Reveals Uninformed Consumers Taking Dangerous Risks with OTC Painkillers," National Consumers League (30 Jan 2003): http://www.nclnet.org/otcpain/jan30release.htm

Cacophony of Jargon: Marketing and Drug Nomenclature

- The marketing of drugs necessarily suffers from some peculiarities of the nature of organic chemistry nomenclature.
- A bewildering and oftentimes confusing array of chemical synonyms, contractions, generic names, trade names, and others.
- One of countless examples:

N-(4-Hydroxyphenyl)acetamide:

aka: 4'-hydroxyacetanilide; p-hydroxyacetanilide; p-acetamidophenol; p-acetaminophenol; p-acetylaminophenol; N-acetyl-p-aminophenol.

- The synonym "N-acetyl-p-aminophenol" begot three major common names:

N-acetyl-*p*-aminophenol ➔ acetaminophen (U.S.)

N-acetyl-*p*-aminophenol ➔ Tylenol™ (U.S.)

(para) N-Acetyl-aminophenol ➔ paracetamol (Europe)

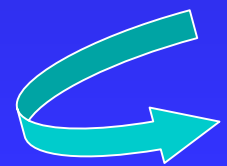
Similar Names Can Lead to Patient-Physician-Pharmacy Confusion

- More than 15,000 formulary names in the U.S. comprising several thousand distinct drug entities.
- Numerous therapeutic categories and hundreds of instances with:

  Similar-looking names (Celebrex vs. Celexa vs. Cerebyx)
  Similar-sounding names (Sarafem vs. Serophene)
  Similar-looking pills (color or shape)
  Similar-looking packaging

  [hundreds of examples at: http://www.usp.org/reporting/prnews/dsw_085.htm]

- Potential for mistakes by patients, physicians, and pharmacists.
- In addition to safety issues, leads to concerns having direct bearing on possible over-consumption of drugs and their unnecessary release to the environment.

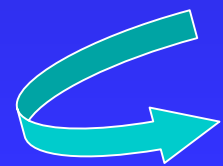


Drug Confusion Can Exacerbate Poly-Pharmacy and Iatrogenic Illness

- Each of the following three common scenarios can result in the unnecessary over-consumption of medication.
- Each presents the potential both for adverse health consequences and for enhanced discharge of drugs to the environment.

iatrogenic = induced in patient by physician's actions

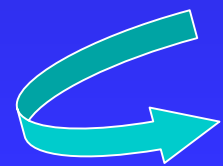
polypharmacy = combined pharmacotherapy (or sometimes called "stacking") by using multiple drugs



Drug Confusion Can Exacerbate Poly-Pharmacy and Iatrogenic Illness

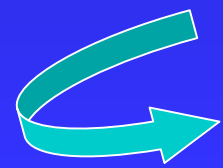
Same drug administered in different formulations: Does presence of same drug entity in different OTC formulations intended for different purposes lead to consumer intake unintentionally higher than recommended? Example: acetaminophen in antihistamines, cough and cold preparations, flu medication, and analgesics.

Different brand names for the same drug intended for unrelated therapeutic purposes: Analogous problem can exist when patient with undisclosed multiple physicians receives prescriptions containing same drug entity (with different names) but marketed for different disorders. Examples: (i) fluoxetine HCl in form of Sarafem (for PMDD) and Prozac (for depression); (ii) bupropion HCl for depression (Wellbutrin), smoking cessation (Zyban), and anorexia nervosa. This problem will grow as multiple therapeutic targets are discovered for existing drugs.



Drug Confusion Can Exacerbate Poly-Pharmacy and Iatrogenic Illness

Iatrogenic Polypharmacy: Different drugs with different therapeutic endpoints but sharing the same side effect: A closely related problem is the prescribing of multiple medications (for a patient with undisclosed multiple specialists) that all share the same common mechanism of action for either the therapeutic endpoint or a side-effect (e.g., anticholinergic syndrome or drug-induced delirium in geriatric patients).



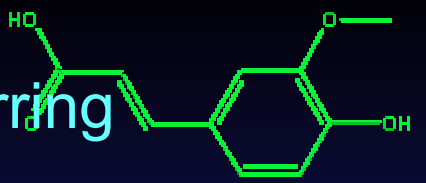
Reduction in Unnecessary Consumption of Medication: One of Many Routes for Reducing Environmental Impact

Polypharmacy and confusion caused by nomenclature are just two of numerous examples where improvements or standardization in procedures could bring multiple benefits to both the consumer and the environment by reducing the over-consumption of medication:

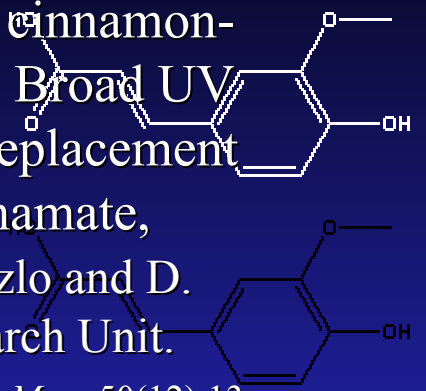
- lower load of drugs to the sewage system via excretion and disposal
- improve therapeutic outcomes by reducing drug-prescribing errors and by reducing adverse drug events (iatrogenic or self-imposed)
- reduce health care expense by reducing overall drug expenditures and lessening need for follow-up treatment

Progress towards international standardization and clarification of drug naming conventions and improved patient information could reduce medication errors, reduce over-dosing, reduce purchase and consumption, and consequently lessen environmental deposition.

Alternative Active Agents: Naturally Occurring

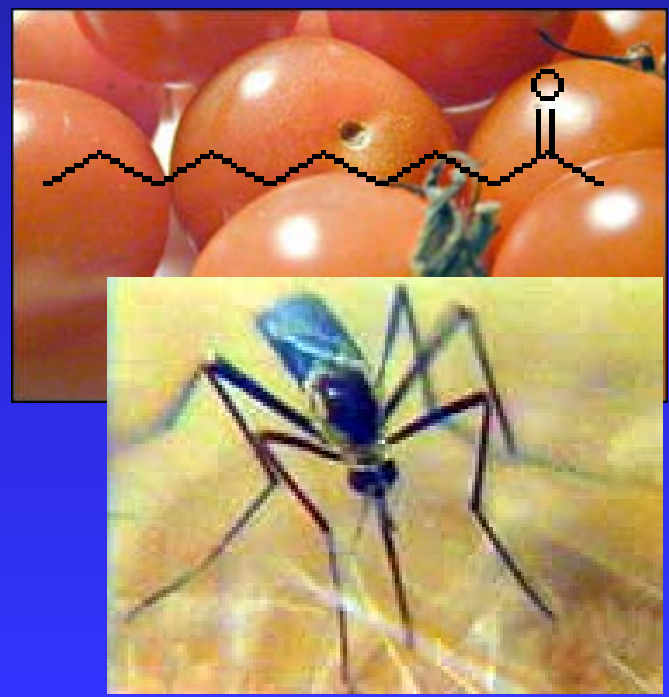


Sunscreen Agent:: SoyScreen™ — made from ferulic acid (a cinnamon-family compound) and soybean oil: feruloylated acylglycerols. Broad UV absorption characteristics over the A, B, & C bands. Possible replacement for all four current sunscreen agents such as octylmethoxy cinnamate, padimate-O, oxybenzone, and dioxybenzone. Research of J. Laszlo and D. Compton, USDA-ARS New Crops and Processing Technology Research Unit.



[see: Suszkiw, J. 2002. "How about some soybeans with that tan?" *Agricultural Research Mag.* 50(12):13; available at: http://www.ars.usda.gov/is/AR/archive/dec02/tan1202.pdf, or http://www.ars.usda.gov/is/AR/archive/dec02/tan1202.htm; also see: http://www.ncaur.usda.gov/nc/079soyscreen.html]

Insect Repellant: Extremely effective repellant for mosquitoes and other insects isolated from tomatoes by Michael Roe (NC State University). 2-Undecanone (IBI-246) licensed to *Insect Biotechnology, Inc.*
First patent: *SkeeterShield.* Alternative to DEET (N,N-diethyl-*m*-toluamide). [see: http://www2.ncsu.edu/ncsu/univ_relations/news_services/press_releases/02_06/164.htm]



Antibiotics: Some Alternatives

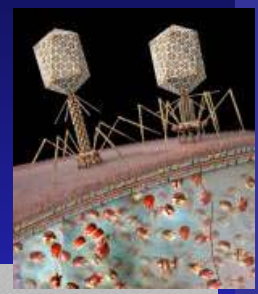
Probiotics & Bacteriophages

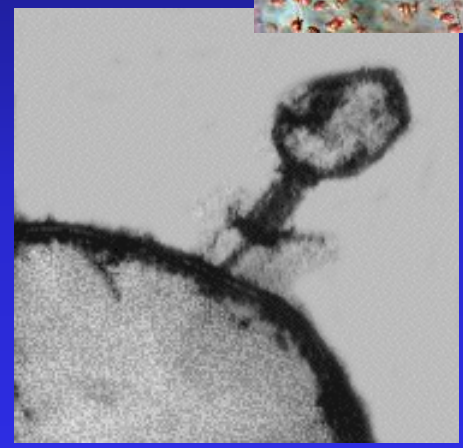
(for "excluding" or killing pathogens)

Probiotics (via pills and food) maintain intestinal flora. New applications include burn treatment.

"Competitive exclusion" products for domestic animals.

Holistic improvement in animal husbandry and hygiene (especially for CAFOs).



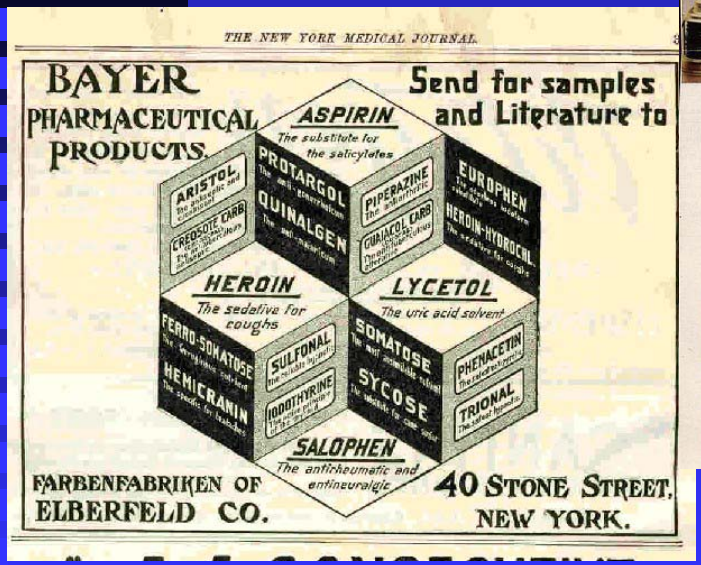


Live "Phage Therapy": pioneered by Soviets in 1920s.

Direct-to-Consumer (DTC) Advertising

- Extremely controversial.
- Banned in most countries (except U.S. and New Zealand).
- Sales Promotion vs. Consumer Education?

Past practices: addictive drugs



oral bacitracin-polymyxin B

Creation of new conditions

Antidepressant Usage: Alternative

FDA approves pediatric use of fluoxetine (SSRI) for depression & OCD (3 January 2003): 7-17 yr-olds
http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01187.html

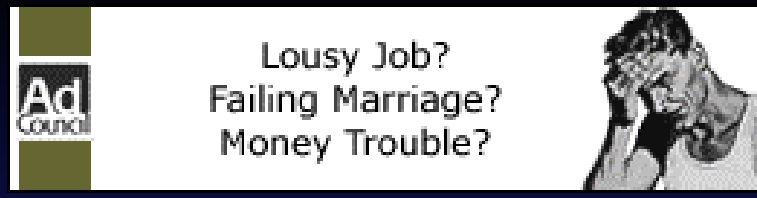
Alternative: Countless controlled studies show profound antidepressant effect of omega-3 food oils: By increasing consumption of the omega-3 essential fatty acid (linolenic acid) coupled with intake of lower ratio of omega-6:omega-3 (e.g., via flax or hemp oils) and augmented intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) [linolenic synthesis products, concentrated in cold-water fish oil].

DTC Advertising *(con't)*:

- Abundance of Controversy
- Ramifications with Respect to Environmental Stewardship Are Unknown

- Grew as a result of FDA 1997 changes in advertising regulation (e.g., only brief mention of side effects required).
- DTC spending more than tripled ($791M to $2.5B) from 1996-2000. Consumer drug costs total over $500B per year.
- Many ask whether DTC interferes with physician-patient relationship (e.g., encouraging "doctor shopping")?
- Creation of unrealistic patient expectations?
- Misleading or incomplete information for consumer?
- Leads to escalation of medication pricing?

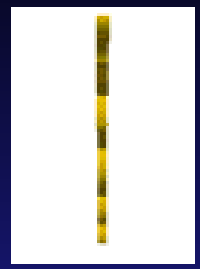
DTC Advertising *(concluded)*:



- Increase prescribing or consumption for previously unrecognized (invented) conditions?
- Leads to unneeded use/treatment?
- Encourages prescription drug use rather than OTC?
- Encourages more expensive new drugs that are only marginally more effective than prior generation?
- Improves healthcare outcomes (via consumer education) or leads to unnecessary increase in drug consumption?
- Past history of marketed drugs includes many now-inappropriate uses (heroin, cocaine, toxic antibiotics, etc.)
- **Never any mention of disposal/recycling of unused drugs**.

[see: "Medicine and Madison Avenue" (Duke University) for comprehensive historical perspective on the commercialization of medicine via advertising: http://scriptorium.lib.duke.edu/mma/]

Near-Term Action: *examples*



Prescribing

- Individualization of therapy (e.g., proactive "calibrated dosing") to minimize dosage amounts. Encourage manufacturers to provide better information to tailor drug dosages to the individual (esp. long-term maintenance drugs) on basis of body weight, age, sex, health status, subtle genetic distinctions, and known individual drug sensitivities. Identify lowest effective dosages ("calibrated dosing").

Many of the issues involved with lower doses (as pertaining to individualized therapy) are summarized in:

"Potent drugs at potent doses cause an epidemic of avoidable side effects," Jay Cohen, *Life Extension Magazine*, March 2003, 47-68.

Near-Term Action: *examples*

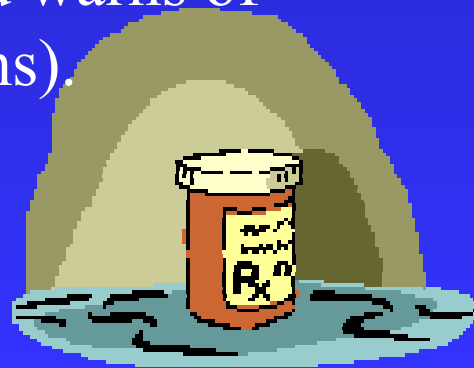
Prescribing (con't)

- Minimize overuse, misuse, imprudent use (involves patient education as well); especially for antibiotics.
- Expand exploration and research of non-chemical alternatives to traditional medications (e.g., reducing/eliminating drug dosages by use of placebos; phage therapy as alternative to antibiotics; probiotics as prophylaxis).

Near-Term Action: *examples*

Dispensing

- Internet Dispensing: Educate/encourage the pharmacy community and the public to better appreciate the environmental consequences of over-dispensing (and dispensing without a prescription). To minimize unneeded drug use and attendant disposal of unused, excess medications [e.g., see: www.fda.gov/oc/buyonline].
- Personal "Medical Statistics Cards": Private electronic card collects data on planned drug purchases and warns of over-consumption (as well as adverse interactions).



Near-Term Action: *examples*

Marketing

- OTC Package Sizes. Consider reducing package sizes of PPCPs. Some PPCPs are perhaps more prone to being disposed because they are prescribed or purchased in quantities too great to be used before expiration or because they tend to expire more rapidly. Encourage eco-friendly, individual blister packaging (to reduce temptation to consume multiple pills at once; the "M&M" effect).

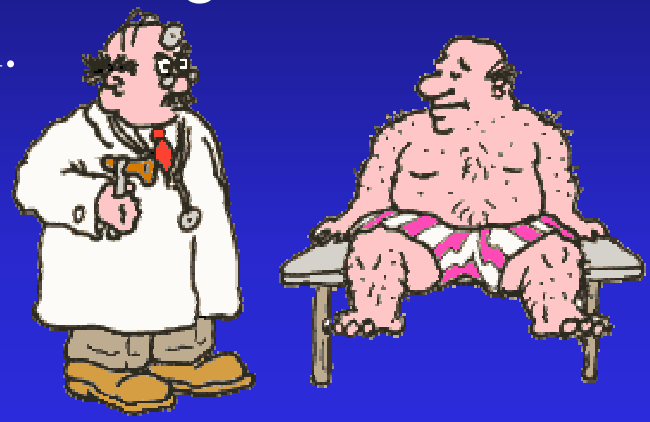
- Prescription Sizes/Duration. Reduce need for disposal by reducing prescribed/purchased quantities too great to be used before expiration, or increasing shelf life.

- DTC for Public Education. Shift emphasis for DTC advertising from sales to consumer education. Include advice for disposal/recycling.

Near-Term Action: *examples*

Consumer/Patient Issues

- **Encourage patient compliance.** Noncompliance by patient can result in prescribed courses of a particular drug to accumulate, leading to the expired/unused dosages to be disposed in the domestic sewage system.



- **Lessen drug abuse.** Consumption of more frequent or higher doses than prescribed (or use of illicit drugs) can increase types and amounts of excreted drugs and metabolites in waterways.

Near-Term Action: *examples*

Design/Manufacturing

- Aim for "environmental friendliness" (green design and innocuous fate).
- Accelerate development of better drug-delivery systems and formulations (e.g., inhalable, dermal -- to minimize dosage).
- Accelerate development of enantiomeric drugs (to cut dosage requirements).
- Develop more ecologically relevant screening tests for new drug candidates (e.g., focus on evolutionarily conserved functions, such as defensive efflux pumps).

Near-Term Action: *examples*

Control

- Disposal: Standardized set of national regulations for disposal of unwanted, expired PPCPs (public, state, and medical, e.g., nursing homes, physician samples).
- Expand scope of "Extended Producer Responsibility" (EPR) (for manufacturers, marketers, distributors, care-givers).
- Outreach efforts for heightening public awareness for recycling alternatives (e.g., public "reverse distributors").
- Source separation for domestic wastes: New technologies for dealing with waste at the source (e.g., separation of streams). Toilet re-engineering is but one example.
- Continue nationwide elimination of straightpiping and septic systems, and minimizing overflow events.

Near-Term Action: *examples*

Disposal

RCRA Re-Evaluation: Periodically re-examine which PPCPs should be considered hazardous under RCRA (e.g., chemotherapeutics can be extremely toxic). This is especially important given continual advancements in design of new generations of drugs.

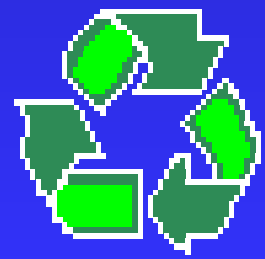
Promulgation of RCRA Requirements: Encourage education of healthcare facilities, pharmacies, drug distributors, and manufacturers regarding current hazardous chemical waste regulations (RCRA) and how to identify pharmaceuticals that are subject to RCRA.

Reverse Distributors: Begin discussions regarding unifying the often conflicting concerns of autonomous regulators (e.g., DEA, EPA, state boards of pharmacy, and others) with regard to the potential for reverse distributors (e.g., take-back programs) in the U.S., especially as extended to the consumer level.

Near-Term Action: *examples*

Prevention: Proactive vs. Reactive

- Encourage purchase of only needed amounts of PPCPs (e.g., reduced package sizes conducive to avoiding expiration).
- Reduce over-dispensing and black market sales of drugs (e.g., "Internet pharmacies").
- Implement use of "drug mining" (e.g., hospital reclamation of highly toxic drugs from excreta and other wastes).
- Expand use of "reverse distributors".



Near-Term Action: *examples*

Prevention: Proactive vs. Reactive

- Shift of primary priority in healthcare toward disease *prevention* and health *maintenance* and away from reliance on treatment of preventable illness with drugs.
- Shift toward reliance on *evidence-based* medicine and away from *unproven* but "accepted" practices.
- Shift toward *curative* drugs that target underlying *causes* of illness, and away from those that merely *suppress* or *mask symptoms*.
- Reduce patients' expectations/demands for medications, and consequently *reduce avoidable iatrogenic illness*.

Near-Term Action: *examples*

Alternative Therapies (Traditional Medicine)

TM/CAM: Traditional, Complementary, & Alternative Medicine

"diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine," for example, including aromatherapy, Ayurveda, dietary supplements, massage, and chiropractic, naturopathic, osteopathic, homeopathic, and naturopathic medicine.

NIH *Office of Alternative Medicine* (OAM) mandated by Congress in 1991 and created in 1993.

NIH *National Center for Complementary and Alternative Medicine* (NCCAM) established within OAM in 1998 as one of the 27 NIH institutes and centers. See: http://altmed.od.nih.gov

Near-Term Action: *examples*

Public Outreach

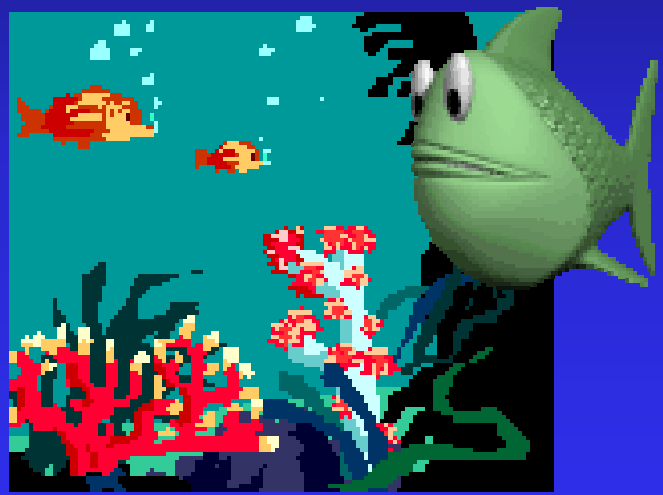
- Recognition that POPs and PBTs represent only a portion of the overall environmental pollutant load.
- Show the health benefits of minimizing overuse/misuse of drugs (e.g., antibiotics).
- Capitalize on occurrence/effects issues to increase public understanding and appreciation for environmental science. Tie actions of the individual to environmental consequences.
- Create materials for public education (esp. via the web).
- Explore possibility of sewage drug monitoring to raise awareness of extent of collective, community-wide drug usage (esp. for illicit drugs and licit drugs of abuse).

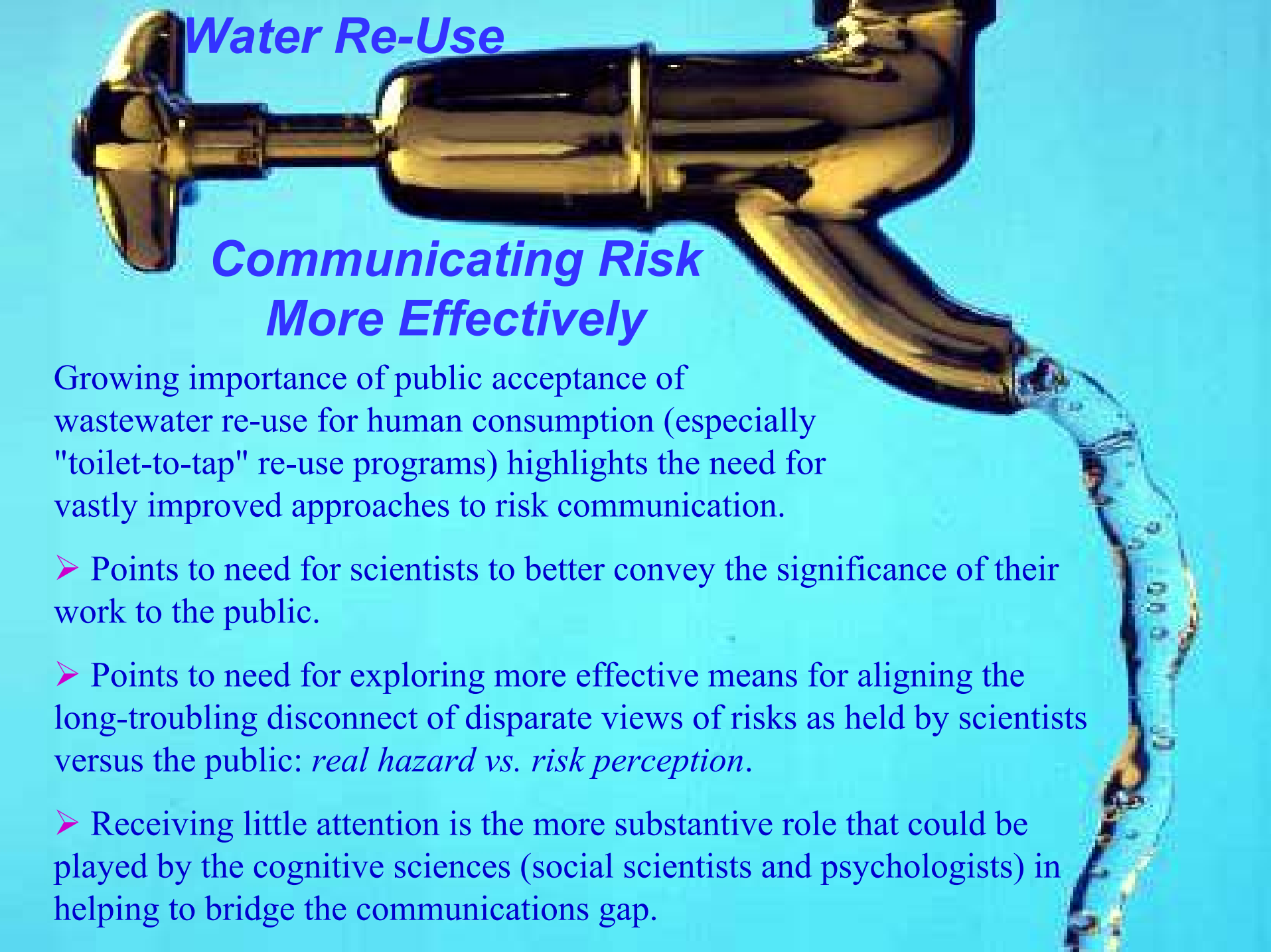
Near-Term Action: *examples*

Fostering Market Penetration

- Patentability: Major impediment to expediting "Green" alternatives
- Many potential "green" alternatives cannot achieve significant market penetration simply because of the lack of market incentive.
- Many alternatives are not conducive to yielding proprietary or patentable products.
- Need alternative mechanism for bringing non-patentable or non-proprietary products to market in the public interest.

Some Concerns Regarding the Future





Water Re-Use

Communicating Risk More Effectively

Growing importance of public acceptance of wastewater re-use for human consumption (especially "toilet-to-tap" re-use programs) highlights the need for vastly improved approaches to risk communication.

- Points to need for scientists to better convey the significance of their work to the public.
- Points to need for exploring more effective means for aligning the long-troubling disconnect of disparate views of risks as held by scientists versus the public: *real hazard vs. risk perception*.
- Receiving little attention is the more substantive role that could be played by the cognitive sciences (social scientists and psychologists) in helping to bridge the communications gap.

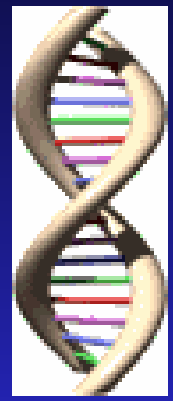
Key to Maintaining & Improving the Public's Confidence in Water Supplies

Implement:

- Cost-effective programs that minimize the escape or disposal to the environment of consumer chemicals such as PPCPs.
- More effective risk communication.
- Chemical monitoring programs that go beyond the conventional approach based on limited target lists of traditional pollutants.
(how much of the total dissolved organic carbon can be accounted for?)

Molecular Farming — Biopharming

- Current transgenic biotechnology has potential for using food crop species (primarily corn, soybeans, rice) for producing hundreds of distinct proteinaceous therapeutics (esp. enzymes, hormones, monoclonal antibodies) by genetically altered plants.



- So-called “molecular farming” or “biopharming” raises host of questions regarding risk, primarily centered around allergenicity and consumer toxicity in the form of direct endocrine disruption or other mechanisms.

- Concerns that are less-discussed, however, include (1) the largely unanticipated hazards presented to non-target organisms, whose interactions with crops are extremely difficult to prevent, and (2) future ability to "pharm" small-molecular non-proteins, which would pose concerns different than those for proteins.

- See discussions at: "http://www.epa.gov/nerlesd1/chemistry/ppcp/relevant.htm#Molecular Farming"

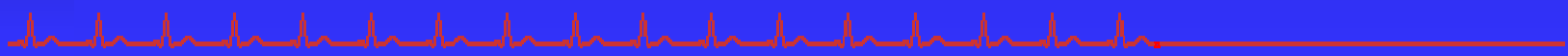
The Ultimate Question

Ultimately, we must ask …

whether an overarching stewardship program (encompassing all aspects of the healthcare industry) aimed at overall reduction in drug usage, recycling, and disposal …

could yield a larger reduction in potential human and ecological exposure for far less investment in R&D and end-of-pipe control technologies, …

and at the same time provide collateral monetary and health benefits for consumers.



Opportunity for Precautionary Action?

The **Precautionary Principle** – the principle of precautionary action that redistributes the burden of proof because the science required for truly and fully assessing risks lags far behind the requisite supporting science.

See links provided at:
http://www.epa.gov/nerlesd1/chemistry/ppcp/relevant.htm#The Precautionary Principle


Don't Let YOUR Drugs Get Away
Prudent & Minimal Usage
Recyling of Unwanted PPCPs

Questions

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